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Workshop on Advances in the Use of Biomarkers in Children

Programme

**HOTEL PANAMERICANO (CROWNE PLAZA) & RESORTS
CONFERENCE ROOM: BUENOS AIRES SALON (GROUND FLOOR)
17-18 NOVEMBER 2005 - BUENOS AIRES, ARGENTINA**

THURSDAY, 17 NOVEMBER – MORNING SESSION

GENERAL INTRODUCTION

Overall Co-chairs:	Dr Terri Damstra - <i>World Health Organization, International Programme on Chemical Safety, Research Triangle Park, North Carolina, USA</i> Dr Bob Sonawane - <i>US Environmental Protection Agency, National Center for Environmental Assessment, Washington, DC, USA</i>	
8:30-8:45am	Welcoming Remarks and Introduction to Prof Dr Her Royal Highness Princess Chulabhorn Mahidol of Thailand Dr Terri Damstra - <i>World Health Organization, International Programme on Chemical Safety, Research Triangle Park, North Carolina, USA</i>	
8:45-9:15am	Keynote Lecture: “The Importance Of Biomarker Research In Children” Professor Dr. Her Royal Highness Princess Chulabhorn Mahidol, <i>Chulabhorn Research Institute, Bangkok, Thailand</i>	
9:15-9:30am	Introduction to Workshop – Biomarkers of Exposure, Effects and Susceptibility in Children’s Environmental Health Dr Bob Sonawane - <i>US Environmental Protection Agency</i>	
BIOMARKERS OF EXPOSURE (AT VARIOUS STAGES OF DEVELOPMENT)		
Co-Chairs:	Dr Lizbeth López-Carrillo - <i>Instituto Nacional de Salud Publica, Mexico</i> Dr Robert Kavlock - <i>US Environmental Protection Agency, Research Triangle Park, North Carolina</i>	
9:30-10:00am	Meconium Analysis for the Detection of Fetal Exposure to Environmental Pesticides Dr Enrique Ostrea - <i>Wayne State University, USA, and University of Philippines, The Philippines</i>	
10:00-10:30am	Biomarker of Fetal Exposure to Multiple Chemicals in Human Umbilical Cords Dr Chisato Mori - <i>Chiba University, Japan</i>	
10:30-11:00am	BREAK	

Workshop on Advances in the Use of Biomarkers in Children

11:00-11:30am	Human Milk as a Pathway of Exposure to Chemicals Dr Fernando Diaz-Barriga - <i>Universidad Autonoma de San Luis Potosí, Mexico</i>
THURSDAY, 17 NOVEMBER – MORNING SESSION (CONTINUED) BIOMARKERS OF EXPOSURE (CLASSES OF CHEMICALS)	
11:30-12:00pm	Biomarkers of Exposure to Air Pollutants Dr Radim Sram - <i>Institute of Experimental Medicine, Czech Republic</i>
12:00-12:30pm	Pesticide Exposure Among Children in Nicaragua: A Pilot Biological Monitoring Study (<i>Spanish Presentation</i>) Dr Teresa Rodríguez Altamirano - <i>Universidad Nacional Autonoma de Nicaragua, Nicaragua</i>
12:30-2:00pm	LUNCH
THURSDAY, 17 NOVEMBER – AFTERNOON SESSION BIOMARKERS OF EXPOSURE (CLASSES OF CHEMICALS AND SUSCEPTIBILITY)	
Co-chairs:	Dr Margaret Karagas - <i>Dartmouth Medical School, USA</i> Dr Fernando Diaz-Barriga – <i>Universidad Autonoma de San Luis Potosí, Mexico</i>
2:00-2:30pm	Exposure of Children and Adolescents to Hazardous Residues in Brazil – A Case Study Dr Carmen Fróes - <i>Universidade Federal do Rio de Janeiro, Brazil</i>
2:30-3:00pm	Biomarkers of Exposure to Metals. The Link Between Markers of Exposure and Susceptibility to Metals Dr Mariano Cebrian - <i>Centro de Investigacion y de Estudios, Mexico</i>
3:00-3:30pm	BREAK
3:30-4:00pm	Variability in Arsenic Methylation: Polymorphisms Associated with Arsenic Metabolism Dr Mercedes Meza - <i>Instituto Tecnológico de Sonora, Mexico</i> (<i>Spanish Presentation</i>)
4:00-4:30pm	Paraoxonase Polymorphisms-Biomarkers of Susceptibility to Pesticides Dr Antonio Hernández-Jerez - <i>University of Granada, Facultad de Medicina, Spain</i> (<i>Spanish Presentation</i>)
4:30-5:00pm	Biomarkers of Pesticide Exposure and their Relation to Health in Children Dr Brenda Eskenazi - <i>University of California, Berkeley, USA</i>

Workshop on Advances in the Use of Biomarkers in Children

6:00pm-8:00pm	POSTER SESSION (W/ REFRESHMENTS)	
<u>FRIDAY, 18 NOVEMBER – MORNING SESSION</u>		
BIOMARKERS OF EFFECT AND USE IN HAZARD IDENTIFICATION		
Co-chairs:	Dr Radim Sram – <i>Institute of Experimental Medicine, Czech Republic</i> Dr Jenny Pronczuk - <i>World Health Organization, Switzerland</i>	
8:30-9:00am	Biomarkers of Cancer in Children Dr Martyn Smith - <i>University of California, Berkeley, USA</i>	
9:00-9:30am	Biomarkers of Effect and Use in Hazard Identification: Lung Function/Asthma Dr Peter Sly - <i>Institute of Child Health Research, Australia</i>	
9:30-10:00am	Biomarkers of Neurobehavioural Effects Dr David Carpenter - <i>University of Albany, USA</i>	
10:00-10:30am	BREAK	
10:30-11:00am	Framework to Use Biomonitoring Data to Inform Exposure Assessment in Children Dr Elaine Hubal - <i>US Environmental Protection Agency, North Carolina, USA</i>	
11:00-11:30pm	Incorporation of Biomarker Data Into Risk Assessment/ Risk Management and Public Health Practices Dr William Suk - <i>National Institute of Environmental Health Sciences, USA</i>	
11:30-1:30pm	PANEL DISCUSSION - PROMOTION OF COLLABORATIVE RESEARCH NETWORKS	
Moderators:	Dr Terri. Damstra – <i>World Health Organization (USA)</i> Dr Jenny Pronczuk – <i>World Health Organization (Switzerland)</i> Dr Mariano Cebrian (Mexico) Dr Fernando Diaz-Barriga (Mexico) Dr Mathuros Ruchirawat (Thailand) Dr P. Mendola (USA) Dr Peter Sly (Australia) Dr Radim Sram (Czech Republic)	
1:30pm	CLOSING OF MEETING Dr Terri Damstra - <i>World Health Organization, USA</i>	

Workshop Presentations

The Importance of Biomarker Research in Children

Prof. Dr. HRH Princess Chulabhorn Mahidol
Chulabhorn Research Institute
Bangkok, Thailand

Children are exposed to a myriad of chemicals in the environment and in everyday life. The contribution of these exposures to childhood illnesses is a public health concern. In many instances, children are at a potentially higher risk for development of disease outcome as a result of these exposures.

It is, therefore, important to be able to identify chemicals children are exposed to, the level of exposure, the potential health effect of such exposure as well as the inherent or acquired ability to respond to the challenge of exposure.

Through the use of various biomarkers, actual exposure, the amount that gets into the body and is able to react at the target organ as well as the resultant effects can be measured.

An example of an extensive study using biomarkers was conducted to assess exposure to carcinogenic compounds in urban air, and potential health effects in children. Through ambient air monitoring and personal monitoring using various biomarkers of exposure and of early effects, the set of information obtained provides conclusive results that city children are at higher risk than other subpopulations of developing diseases such as cancer as a result of exposure to carcinogenic compounds such as polycyclic aromatic hydrocarbons and benzene in ambient air on a daily basis. Children seem to be more sensitive to the DNA-damage effect of carcinogenic compounds and their ability to repair the genetic damage seems to be lower than adults.

Biomarkers of Exposure, Effects and Susceptibility in Children's Environmental Health

B. Sonawane; N. Keshava; and S. Barone

**National Center for Environmental Assessment, Office of Research and Development, U.S. Environmental Protection Agency
Washington, DC**

Biomarkers are early indicators of health hazards in response to exposure to environmental stressors. Historically, biomarkers are used for diagnosis of a disease, however, their application is relatively new in environmental health, especially in understanding risks associated with low level environmental exposures, and more specifically in pediatric population. Biomarkers have the potential to be quantitative dosimeters of exposure and toxic response. They can provide insights into mode(s) of action at biochemical and cellular level. Biomarkers can be used to monitor a wide variety of responses ranging from abnormal development to early indicators of the disease. Biomarkers of exposure are typically measured in surrogate tissue such as blood, milk, urine, saliva, nail, hair, amniotic fluid, and meconium. Growing evidence shows that fetuses, infants and children are more vulnerable than adults to a variety of environmental insults because of their physiological immaturity, and differential exposure. Genetic susceptibility and environmental exposures during critical periods of development are likely to contribute to adverse outcomes in childhood and later life stages. Advances in technology may have important implications for the early detection, prevention and treatment of certain diseases in children. However, biomarkers need to be validated for their specificity and sensitivity to be useful in risk evaluation. When appropriately used in hazard characterization, and dose-response analysis, biomarkers may replace default assumptions used in inter-individual human variability, species, route and dose extrapolations.

Disclaimer: The views expressed in this abstract are those of the authors and do not represent U.S. EPA policy or endorsement.

Meconium Analysis for the Detection of Fetal Exposure to Environmental Pesticides

E.M. Ostrea, Jr., Bielawski, N.C. Posecion, Jr., Corrion, Y. Jin
Hutzel Hospital, Wayne State University,
Detroit, MI

Background: Exposure of pregnant women to environmental pesticides may be harmful to the developing fetus.

Objective: The aim of this study was to determine the best matrix to analyze and detect fetal exposure to these toxicants.

Design/Methods: Pregnant women were prospectively recruited at midgestation from an agricultural site in the Philippines where our preliminary survey showed significant use at home or in the farm of the following pesticide/herbicide: cyfluthrin/propoxur (73%), chlorpyrifos (37%), cypermethrin (31%), pretilachlor (28%), bioallethrin (26%), malathion (15%), diazinon (12%) and transfluthrin (11%). Maternal hair and blood were obtained upon recruitment [hair A (n=890), blood A (n=886)] and at birth [hair B (n=766), blood B (n=762)]. Umbilical cord blood (n=582), infant hair (n=503) and meconium (n=554) were obtained at birth. All samples were analyzed for the above compounds by GC/MS.

Results: Analysis of meconium detected the highest fetal exposure rate (% positive) to the toxicants: propoxur (27.62%), diazinon (0.18%), malathion (0.36%), bioallethrin (0.36%), pretilachlor (1.99%), DDT (0.54%) cyfluthrin (0.54%) and cypermethrin (2.17%). Cord blood was only positive for propoxur (2.06%) and infant hair for propoxur (0.20%) and chlorpyrifos (0.20%). By meconium analysis, 40% of the infants were exposed to 1 pesticide and 3% to 2 pesticides. Maternal hair showed the next highest exposure rate, particularly in samples taken at delivery: propoxur (13.3%), chlorpyrifos (0.11%), bioallethrin (8.99%), pretilachlor (0.11%) and DDT (0.22%). High exposure to propoxur was due to common use of spray insecticide (Baygon) at home by pregnant women (43%)

Conclusions: Prenatal exposure to environmental toxicants is best detected by the analysis of meconium and maternal hair. However, maternal hair results probably represent passive exposure. Since meconium is fetal in origin, it represents the best matrix to detect fetal exposure to environmental toxicants.

[Supported by grants from NICHD (1R01HD039428001A1) and USEPA (RFA 2001-STAR-H1) No. R829395-01-0].

Biomarker of Fetal Exposure to Multiple Chemicals in Human Umbilical Cords

Chisato Mori

**Department of Bioenvironmental Medicine; Environmental Health Science Project for future generations, Graduate School of Medicine, Chiba University; Center of Environmental Health Science for future generations (NPO)
Chiba, Japan**

Human fetuses are at a high-risk life stage in human life and our studies analyzing umbilical cords (UCs) or cord serum show that human fetuses are exposed to multiple chemicals. Human UC is a part of the fetal tissue. Using UCs, we have carried out an analysis of chemical exposure level and a global analysis of gene expression level. We detected dioxins, PCBs, DDTs, DDEs, chlordanes, hexachlorobenzene, hexachlorocyclohexane, heavy metals, and phytoestrogens. Total PCB and p,p'-DDE were detected from all the UCs at higher concentration levels. The fetuses that accumulated PCB at higher levels had a tendency to accumulate other chemicals at higher levels. We also found a positive correlation between the concentration of total PCBs in mother serum (MS) and the sum of concentration of environmental persistent chemicals in UCs. Moreover, the gene expression profile of UCs can detect a potential high risk group from the actual high exposure and the genetic high susceptibility to multiple chemicals during fetal period. In this presentation, I summarize the results of our fetal exposure assessment using UCs/MS in current Japanese babies and mention that toxicogenomic analysis of human UCs could be used as a new risk assessment to detect potential high-risk group from the view of exposure level and susceptibility. The purpose of my presentation is to introduce our attempts to find the potential high-risk group in the next generation, in order to prevent the long-term effects caused by fetal exposure (exposure at high-risk life stage) to multiple chemicals.

Human Milk as a Pathway of Exposure to Chemicals

O.D. López-Guzmán, L. Yañez, E. García-Nieto, R. Costilla-Salazar, I. Pérez-Maldonado, and F. Díaz-Barriga

**Departamento de Toxicología Ambiental, Facultad de Medicina, Universidad Autónoma de San Luis Potosi
México**

Human milk is the best source of nutrition for infants. Breast milk contains the optimal balance of fats, carbohydrates, and proteins for developing babies, and it provides a range of benefits for growth, immunity, and development. Unfortunately, breast milk is not pristine. Contamination of human milk is widespread and is the consequence of decades of inadequately controlled pollution of the environment by toxic chemicals. The finding of toxic chemicals in breast milk raises important issues for pediatric practice, for the practice of public health, and for the environmental health research community. This is the case for children living in contaminated areas, for example we have found higher levels of dioxin in milk samples of women exposed to biomass combustion or in women living in chemical areas; furthermore, we found high levels of DDT and its metabolites in samples of women living in malarious areas where this insecticide was used. In malarious areas, children have higher levels of DDT in blood than adults. Thus, at least in these examples, a surveillance program is needed for children that are exposed to chemicals through human milk ingestion.

Biomarkers of Exposure to Air Pollutants

R.J. Sram

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The molecular epidemiologic studies suggest biologic mechanism for the effect of air pollution on birth outcomes. It has been shown that the levels of DNA adducts are positively related to risk of IUGR, birth weight, birth length, health circumference, and hypoxanthine-guanine phosphoribosyl-transferase locus (HPRT) mutation frequency in infants. The finding of higher DNA adduct levels in the infant compared to the mother suggests an increased susceptibility of the developing fetus to DNA damage. The level of DNA adducts is associated with genotypes. With respect to IUGR, it appears that the increased risk is principally due to exposure to carcinogenic PAHs (c-PAHs). Air pollution by c-PAHs also increased the frequency of micronuclei in the children peripheral lymphocytes. Polymorphisms of metabolic genotypes (GSTM1, GSTP1, GSTT1, EPHX3, EPHX4, CYP1A1 Ile/Val and CYP1A1-MspI) affected birth weight as well as the category low birth weight (<2500 g) + prematurity (< 37 weeks). The genetic polymorphisms (DNA repair genes XPD exon 6 and XRCC1) also influenced the lower respiratory illness in preschool children. The presented results indicate the necessity to use complex approach of using biomarkers of exposure, effect and susceptibility to analyze the impact of air pollution to children health as well as to utilize obtained data for the risk assessment.

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Pesticide Exposure among Children in Nicaragua: A Pilot Biological Monitoring Study

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In Nicaragua and elsewhere in the developing world, children are exposed to pesticides through various pathways. Children that live in close proximity to farms, and children whose parents are agricultural workers have higher exposures to pesticides. There are two major purposes of this study: (1) Describe exposure to the organophosphorus pesticides of pesticide applicators and children that live with them in the area around León, Nicaragua, and (2) Develop alternative biomarker for population-based study focusing on children. A total of 17 families were recruited to participate in the cross sectional study. A family consists of a pesticide applicator and a child residing together. The ages of children under this study ranged between 2 to 12. Blood, saliva and urine samples were collected from the adults the day before application, the day of application and the day after the application. Saliva and urine samples were collected from the children over the same three-day period. Urine samples aliquot in Nicaragua were shipped to the Center for Disease Control and Prevention (CDC) in Atlanta, GA, blood and saliva samples were shipped to University of Washington, WA. This abstract will address only the data obtained from the children samples. The specific chlorpyrifos metabolite 3,5,6-TCPY (<LOD to 125.13 ug/L), the general pyrethroid metabolites 3PBA (<LOD to 4.36 ng/mL) and 4F3PBA (<LOD to 1.08 ng/mL), the metabolite for permethrin, cypermethrin and cyfluthrin Trans-DCCA (<LOD to 5.13 ng/mL) were quantified in urine samples. Diazinon was found in 20 of 49 (41%) saliva samples collected from children.

Exposure of children and adolescents to hazardous residues in Brazil – a case study

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Introduction: Cidade dos Meninos is an area in the State of Rio de Janeiro / Brazil, where a factory of formulation and storage of organochlorine pesticide worked from 1950 to 1961. The chemical wastes generated were released in the area and the inhabitants have come into contact with these toxic substances. The aim was to determine and characterize risks from exposure to organochlorine pesticide wastes in Cidade dos Meninos.

Method: The public health assessment process of the Agency for Toxic Substances and Disease Registry was used. It was calculated the exposure dose by food ingestion (eggs and milk) and soil (dust) considering the environmental contamination data for children up to 11 years. To know if the contaminants are likely to pose a health threat in the Cidade dos Meninos exposure conditions, the data collected were compared with Minimal Risk Levels (MRL and RfD – Reference Dose) for the noncarcinogenic effects. Carcinogenic effects had been investigated too.

Results: The following contaminants of interest were identified: Hexachlorocyclohexane (HCH) and its isomers, Dichlorodiphenyltrichloroethane (DDT) and its metabolites, Trichlorobenzenes, Trichlorophenols, Dioxins and Furans. For all compounds identified, except trichlorophenols, the exposure doses are superior to the minimum risk levels for chronic exposure of children. For the isomers of HCH the acute and chronic MRLs are surpassed by the children's exposure dose. The estimated exposure dosage for dioxins surpass in over 100,000 times the minimum risk value for children.

Conclusion: The Cidade dos Meninos poses an urgent public health hazard because of high and serious exposure to persistent organic pollutants. The assessment of risk to health is an important tool for decisions of public health.

Biomarkers of Exposure to Metals. The Link Between Markers of Exposure and Susceptibility to Metals

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We have explored the link between markers of exposure and susceptibility to As and Pb in Region Lagunera, Mexico, where several circumstances have resulted in increased health risks derived from chronic arsenic and lead exposure in children. Regarding lead exposure, we studied the influence of ALAD genotype on biomarkers of exposure (PbB levels) and effect (Blood ZPP) in children living in Torreon. A significant increase in the odds ratio (OR) for the effect of lead exposure on ZPP levels was observed for ALAD^{I-1} children having PbB values above 20 µg/dL, as compared to those having PbB levels below 10 µg/dL, whereas no significant increases were observed for the ALAD^{I-2/2-2} children. Our results suggested that heme biosynthesis was less affected in ALAD^{I-2/2-2} lead exposed children than in those carrying the ALAD^{I-1} genotype. Regarding arsenic, our aim was to study the urinary excretion of As metabolites in children living in the rural area of the Region, since alterations in the urinary profile of arsenic metabolites in adults was shown to be associated with the presence of precancerous skin lesions. There was an increasing percentage of Asi and methylarsonic acid (MMA) and a corresponding decrease of dimethylarsinic acid (DMA) excreted in urine, associated to increasing concentrations (100 to 1,250 µgAs/L) of TAs. This suggests that high chronic arsenic exposure decreases children's ability to methylate Asi to MMA and DMA.

Variability in the Arsenic Methylation: Polymorphisms Associated With Arsenic Metabolism

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Individual variability in arsenic metabolism in humans has been reported frequently. Recent studies have shown genetics as the key contribution for the variation in the arsenic methylation. Thus the objective of this investigation was to study the association between urinary arsenic metabolite levels with 23 polymorphic sites on three arsenic metabolite candidate genes, *PNP*, *GSTO* and *CYT 19*. Subjects (135) from the Yaqui Valley, Sonora, Mexico, who were exposed to arsenic in their drinking water in concentrations ranging from 5.5 to 43.3 ppb were examined. Polymorphisms in the genes of interested were evaluated relative to the ratio of urinary inorganic arsenic [As(III)] to inorganic arsenic [As(V)] and the ratio of urinary dimethylarsenic [DMA(V)] to monomethylarsenic [MMA(V)]. In the initial association screening, three polymorphic sites in the *CYT 19* gene were significantly associated with DMA/MMA ratios in the total population. Posterior analysis of this association revealed that the association signal for the entire population was actually caused by an extremely strong association in only the children (7-11 years of age) between *CYT 19* and DMA/MMA levels. With children removed from the analysis, no significant genetic association was observed in adults (18-79 years). No association was found between the urinary arsenic metabolites levels and the other polymorphic sites in the *GSTO* gene, whereas some polymorphic sites in the *PNP* gene were associated with the As(III)/As(V) ratio in the general population. The existence of a strong, developmentally regulated genetic association between *CYT 19* and arsenic metabolism carries import for both arsenic toxicology and public health.

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Paraoxonase Polymorphisms-Biomarkers of Susceptibility to Pesticides

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Paraoxonase-1 (PON1) is a protein synthesized primarily in the liver and secreted into the blood where it is associated with HDL particles. It catalyzes a number of synthetic and natural substrates, the most known being active metabolites of several organophosphorus (OPs) esters (paraoxon). PON1 has also been implicated in the detoxication of oxidized lipids and in the metabolism of some drugs. Earlier studies observed a polymorphic distribution of plasma PON1 in human populations with either bi- or trimodal distributions, so that individual with low, intermediate or high paraoxonase activity could be identified. This distribution was further related with the differential sensitivity of individuals to OPs, supporting a role for the enzyme as a susceptibility biomarker. Several epidemiological studies have examined the involvement of PON1 in xenobiotic susceptibility in different scenarios: Gulf War veterans, sheep dippers, acute poisoning with OPs and chronic exposure to pesticides in intensive farming. In this Workshop the major results of different studies carried out in plastic greenhouses from Southern Spain are presented. Briefly, carriers of the PON1-192R allele had lower serum and erythrocyte cholinesterase activities, while at the same time they were protected against a previous episode of pesticide poisoning. On the other hand, PON1 is not only an individual marker of susceptibility, but also a biological indicator of exposure to pesticides as a decreased activity was observed in workers spraying these agents. In conclusion, the cumulated evidence supports a role for the determination of PON1 functional genotype in the surveillance of individuals occupationally exposed to pesticides.

Biomarkers of Pesticide Exposure and their Relation to Health in Children

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CHAMACOS is a longitudinal birth cohort study of pregnant women and children living in the agricultural community of the Salinas Valley, Monterey County, California. The CHAMACOS cohort includes primarily low-income Mexican immigrant farmworkers and their families. The aims of CHAMACOS include assessment of: 1) exposure to pesticides and agricultural agents in pregnant women and young children; 2) the potential health effects of pesticides on childhood growth, neurodevelopment and respiratory disease; and, 3) the mechanisms of pesticide neuro- and immuno-toxicity. We also have developed community-based interventions to reduce take-home pesticide exposure to children of farmworkers. We interviewed the mothers (during pregnancy and at all visits), conducted neurodevelopmental assessments (at 6, 12, 24, 42 and 60 months) and housing inspections, and collected numerous biologic and environmental samples. We have found that pregnant women in the CHAMACOS cohort had higher levels of exposure to organophosphate (OP) and some organochlorine (OC) pesticides than in the general US population. We have reported an association of OP pesticide metabolites in maternal urine with shorter gestational duration and with abnormal reflexes in the neonate. We have completed analyses of paraoxonase (PON1) genotype and activity in 130 mother/newborn pairs and have shown that newborn children had much lower levels of PON1 enzyme activity compared to mothers, suggesting greater susceptibility to the effects of OP pesticides. We will present additional findings of the relationship of OC exposure and other health outcomes in these children.

Biomarkers of Cancer in Children

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Cancer is the leading disease killer of children in Western countries and there are thousands of cases in the developing world that go largely untreated. Leukemia is the most common form of cancer in children. We are attempting to find the causes of childhood leukemia using a molecular biomarker approach. Using molecular analysis of DNA from Guthrie Card blood spots taken at birth we have established that most cases of childhood leukemia begin *in utero*. Thus, exposures to the fetus during pregnancy are likely to be critical and we are exploring adduct measurements in Guthrie Cards as biomarkers of fetal exposure. Indeed, exposure to indoor pesticides during pregnancy and the first year of life raises leukemia risk. Analysis of genetic polymorphisms may provide clues to environmental factors associated with cancers in children. For example, at least two studies now show that the inactivating *NQO1 C609T* polymorphism is positively associated with leukemias arising in the first 1-2 years of life and polymorphisms in the *MTHFR* gene have been associated with adult and childhood ALL. Thus, low folate intake and compounds that are detoxified by the quinone oxidoreductase NQO1 may be important in elevating leukemia risk in children. We have also explored the use of proteomics to sub-classify leukemia, because cytogenetic analysis is costly and time-consuming. Several proteins have been identified that may serve as useful biomarkers for rapidly identifying different forms of leukemia. Finally, we would encourage the development of an international consortium to study childhood leukemia and other childhood cancers.

Biomarkers of Effect and Use in Hazard Identification: Lung Function/Asthma

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Young children are especially vulnerable to the effects of inhaled pollutants and air toxics. This is due, in part, to the rapid growth and development of the lungs taking place during the first 2 years of life. In addition, factors increasing susceptibility include: greater lung surface area to volume ratio, greater minute ventilation and smaller airway caliber. The adverse effects of environmental hazards on the lungs include: alterations in lung growth, alterations in airway branching patterns, airway inflammation, an increased susceptibility to respiratory infections and the development of inflammatory lung diseases such as asthma. Potential biomarkers of these effects include: measurements of structural effects, e.g. lung volumes, lung function and bronchial responsiveness; indicators of airway inflammation, e.g. exhaled nitric oxide, oxidative stress markers in exhaled breath condensates, sputum, blood or urine, inflammatory cells and pro-inflammatory cytokines in sputum, blood or urine; and indicators of lung destruction, eg measurement of elastin and collagen breakdown products in the urine. The major problems in applying these biomarkers to studies of the environmental impact on children's respiratory health include: the age of the child - the most informative studies will include children from birth and measurements in the first years of life; many of the techniques are not really suitable for field studies and some are relatively invasive or beyond the developmental capacity of young children.

Biomarkers of Neurobehavioral Effects

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Lead, methyl mercury, PCBs and some pesticides all are well documented to cause reductions of IQ of up to about 5-7 IQ points and behavioral effects, such as shortened attention span and increased antisocial behavior. The magnitude of the neurobehavioral effect is in general a function of the concentration of the contaminants at the time of harm. While all of these contaminants are somewhat persistent, they vary in their half-life in the human body. Therefore contaminant levels determined at older ages will not always reflect levels present in young children at the time they are most vulnerable to damage. Lead has a residence time in whole blood of 1 month, but is stored in bone where it has a residence time of up to 25 years in cortical bone. Therefore blood lead, usually measured as erythrocyte protoporphyrin, detects current exposure, while bone lead is a good measure of exposure over a long period of time. Methyl mercury has a half-life in the human body of 70 days, and can be measured either in blood or in hair. Methyl mercury and inorganic mercury bind to proteins throughout the body, but methyl mercury is more able to cross into the brain than inorganic mercury. PCBs and organochlorine pesticides are fat-soluble substances, and are stored in body fat. While they are best determined by a fat biopsy, they are usually measured in blood, where they are dissolved in the lipid layer. Often results are reported as "wet-weight", which is on the basis of blood volume, but they are also sometimes reported as "lipid-adjusted", which is the concentration found in the lipid layer. These compounds have very long half-lives (about 7-10 years). Because the developing fetus is most vulnerable, measurements of levels in pregnant women or new mothers may provide the most important biomarker of exposure to the child.

Framework to Use Biomonitoring Data to Inform Exposure Assessment in Children

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The US EPA is being called on to assess cumulative risk resulting from exposures to multiple stressors. The Agency is also being required to identify vulnerable populations, characterize life-stage risks, and evaluate gene-environment interactions. The use of biomonitoring data holds a great deal of promise for characterizing exposure and informing cumulative risk assessment. Currently, however, there are significant challenges associated with estimating and interpreting toxicant exposures and health risks from biomonitoring data. Though low levels of environmental contaminants can be measured in tissues of children and fetuses, it is not always known whether the measured exposure leads to an adverse health outcome. In addition, information on exposure pathways is often required to link biomonitoring results to contaminant sources and to reduce exposures and risks. Application of biomonitoring to inform our understanding of the complex relationships between environmental exposures, individual vulnerability, and health outcomes requires sound scientific understanding of the systems that are being assessed and appropriate tools for characterizing these systems. A framework is presented to provide the conceptual basis for considering biomonitoring data and other health metrics in assessment of cumulative exposure and risk. In this framework, biomonitoring and other health data are used to characterize the receptor (individual, community or population), potential exposures, and health outcomes. By considering an array of metrics across the exposure-outcome continuum, this framework begins to address the multi-factorial nature of environmental disease and cumulative risk. Examples will be presented to demonstrate application of this framework to inform exposure assessment and characterize cumulative risk.

Disclaimer: Although this work was reviewed by EPA and approved for publication, it may not necessarily reflect official Agency policy.

Incorporation of Biomarker Data Into Risk Assessment/ Risk Management and Public Health Practices

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Major diseases confronting us today are chronic and disabling conditions. These diseases are the largest cause of death worldwide, led by cardiovascular disease and followed by cancer, chronic lung diseases, and diabetes mellitus. The prevalence of common diseases is increasing. In developing countries, where common diseases have not displaced acute infectious disease, a protracted double burden of disease exists, and whereas public health practices have centered on infectious disease, the expanding public health burden from common diseases has been the subject of relatively modest attention.

The risk assessment process helps to define exposures of concern and potential threats. The more robust the risk assessment, the better one is able to contribute to cost-effective and yet protective choices. The synthesis of environmental health knowledge resulting from research ultimately should contribute to the robustness of the risk assessment process. Scientific inquiry that supports a paradigm whereby knowledge gained through understanding disease processes resulting from environmental exposures would further our understanding of potential human health effects, provide a creative, holistic approach to integrate seemingly separate biological systems, ecological and human health risk assessments into more comprehensive model. However, to fully realize the benefits from such conducted research, especially as it pertains to issues of susceptible populations, low dose effects, mixtures and ecological studies, a new generation of risk assessment models is required.

It is clear that environmental factors, in combination with genetic factors, play a huge role in common disease susceptibility. Associations between environmental factors and health outcomes are, however, complex and poorly characterized. Levels of exposure, for example, are often difficult to ascertain, owing to a lack of detailed biomonitoring as well as to inevitable variations within any population. New technologies and genomic information, however, promise to meet this long-standing challenge. Common diseases require an understanding of gene-gene, gene-environment, and gene-vector-environment interactions. With the advent of the high-throughput techniques of genomics, proteomics, and metabolomics, biomedical science has been steadily shifting to a more comprehensive focus on understanding the diverse and complex responses underlying the development of disease. Coupled with increases in computational power and sophisticated informatics tools for data integration and modeling, researchers can develop quantitative models to help determine the uncertainty of risk. These efforts would fulfill the promise of molecular biomarkers bringing them from the laboratory environment to the clinical/population-based setting, where they can have their intended impact on reducing the burden of human disease and protecting susceptible individuals from adverse and unnecessary risk.

Internationally Harmonized Longitudinal Children Studies: Biological and Environmental Measurements

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Recent recognition of the special susceptibility of children to environmental hazards calls for the establishment of *longitudinal cohort studies* (LCS) that specifically investigate the child's health and environments. Such studies, currently undertaken in North America and Europe, are needed in low and middle income countries. Over three million children under the age of five die every year, mainly in developing countries, as a result of unhealthy air, water, and other environmental hazards. LCS provide an increased understanding of and identify solutions to the impact of the environment on the health and development of children who suffer infections, malnutrition, and other consequences of persistent poverty.

An International Interest Group (IIG) chaired by representatives of WHO and NIH/NICHD is promoting inter-country cooperation on the implementation of LCS in low and middle income countries. Internationally harmonized studies are based on cooperative research plans, common hypothesis formulation and standardized core protocols, including agreements on the main measurements and biomarkers of exposure. This international initiative will not only allow the collection of a large pool of harmonized data, but also the use of new techniques for the detection of biomarkers of exposure, of genomic and proteomic studies and of innovative analytical methods for measuring environmental pollutants. The implementation of LCS requires mechanisms for data quality assurance, control and harmonization, and collection/banking of biological samples.

The IIG is working on six basic study hypothesis, dealing with: *respiratory effects, pregnancy outcome and birth defects, neurodevelopment, growth and development, and cancer*. The biological samples required for these studies include: mother's blood and urine; cord blood; child urine; breast milk, hair and teeth (placental, amniotic fluid, meconium and faecal samples being of lesser value). Consideration is given to sampling for cell lines, for DNA and other studies. It is important to consider the new "omics" methods (transcriptomics, proteomics and metabolomics), the study of susceptibility factors, of genes involved in activation, detoxification and DNA repair and the important effects of diet.

A number of environmental samples are required. A table of environmental risk factors (categorized as chemical, physical, social and other) is available and a matrix that summarizes the (a) clinical assessments, (b) biological sampling and (c) measurements to be done during pregnancy, at the time of delivery and weekly/monthly, up to age 5 (or more) is presented. The importance of a detailed environmental questionnaire is underscored.

LCS are complex due to the logistics required and the myriad of measurements involved. However, they are very valuable for demonstrating the relationships between multiple environmental and non-environmental exposures and multiple outcomes, and for allowing to explore the effects of cumulative exposures on the health and development of children across various stages of development. Internationally harmonized LCS will increase attention and awareness about the harmful environmental influences on children's health and help reduce the burden of environmentally-related pediatric diseases throughout the world.

A Strategy to Develop Environmental Sciences and Toxicology in Mexico: The U.S.-Mexico Bi-national Center

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The North American Free Trade Agreement has successfully increased trade between U.S. and Mexico. However, a number of concerns have come to light about environmental health and hazardous waste pollution in the Border States. In particular, hazardous pollutants from 3,000 border industries (*maquiladoras*), intensified pesticide usage, as well as wastes from mines and metal processing have had demonstrable health impacts. A lack of trained human capital to plan, implement, and maintain environmental infrastructure has been identified as a major obstacle for Mexico in its effort to face the growing environmental and public health challenges.

Our strategy to develop environmental sciences and toxicology is to create a higher education partnership between the University of Arizona (UA) and a consortium of ten Mexican Universities/Institutes and anchor the higher education partnership into a long-term commitment as part of the Binational Center for Environmental Sciences and Toxicology between Mexico's Science and Technology Ministry (CONACYT) and the UA. The main objectives of this partnership are: 1) Build capacity among Mexican graduate students and faculty to solve problems related to hazardous pollution in Mexico; 2) Support the development of Mexican degree programs in this area; 3) Foster research collaboration between UA and Mexican faculty. A multidisciplinary approach will be implemented by integrating public health, toxicology, and environmental engineering, modeled upon NIEHS Superfund Basic Research Program. The project will be carried out through four major kinds of activities: 1) Fellowships for graduate studies; 2) Providing short courses; 3) Developing educational materials; and 4) Research projects. Environmental problems common to both the US and Mexico should serve as the focus for the capacity building program and collaborative research. Four common environmental problems were identified for phase one: 1) Arsenic in drinking water; 2) Impact of mining/metal processing on public health; 3) Pesticide use and health impacts; and 4) *Maquiladoras* and uncontrolled disposal/release of toxic substances. The most important outcome of this project will be the creation of human capital with multidisciplinary training in the areas of environmental science, engineering, and toxicology.

Poster Session

Study of Environmental Lead Contamination in Children in the Area Around Jujuy, Argentina

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The objective of this study was to evaluate the exposure of children from Abra Pampa, to environmental lead, which comes from an old smelting factory, located in the urban area of this city, that was opened until the late 1980's, and from where the mineral has not been removed, so it still remains out in the open.

The research was made using 144 blood samples from 5 to 16-year old children, both male and female, which represented 3.3% of the children population of Abra Pampa. In all of the samples, the activity of the enzyme ALA Dehydrase was determined (standardized European method) and in 25 of the samples, the lead blood levels were determined (atomic absorption - electro-thermal atomization).

Of the 144 samples that were studied, 3.5% showed values of ALA D inferior to the reference values (21 U/L). In 40% of the cases studied (N = 25) lead blood levels were above the 10 ug/dl recommended by the CDC. The highest level found was 41.3 ug/dl in a 5-year old child.

The fact that we found high lead blood levels indicates that the environmental pollution still continues despite the closing of the factory, it also supports the need to fully eradicate it, as well as the need to make clinical and toxicological studies that include the risk population (children and pregnant women, mainly) in order to prevent and/or treat the multiple adverse effects provoked by the metal.

Evaluation of the Inhibition of the Enzyme Acetilcolinesterasa in Childlike Rural Population Exposed to Insecticides from Jujuy

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The objective of the study was to determine and to compare the concentrations of the Acetilcolinesterasa eritrocitaria and plasmática in children exposed to inhibiting insecticides of the colinesterasa and in children done not expose. 44 exposed children were studied from Yuto and 37 not expose children from Leon, localities of Jujuy. They were individuals of both sexes between 7 and 10 years with a minimum residence of 3 years in the place. A medic evaluation, survey to the parents and physical exam with measurement of size, weight, evaluation of hearing and vision was carried out to them. The levels of colinesterasa plasmatica for the population of Leon are in the rank of the normal values, being the value average of 5.181 ± 1.047 U/L. In Yuto the 80% of the samples present normal values, the 20% remaining shows inhibition of the enzyme. The value average for this population is 4.213 ± 1.031 U/L. The colinesterasa eritrocitaria in the 11% of the samples from Leon presents values under the normal values and in the 23% for the population from Yuto. The inhibition of the enzymes do not surpass the 30% of the activity. Statistically significant differences exist in the values of both colinesterasas among the population control (Leon) and the studies one (Yuto). The results permit to confirm that the children from Yuto are exposed to inhibiting of colinesterasa, a situation of high risk. The value average of the enzyme eritrocitaria for this population is next to the normal lower limit, this population would be able to pass to the category of "poisoned chronic". The hypothesis about the damages in the childlike health is reinforced produced by the excessive use of insecticides organofosforados and carbamicos in some rural zones in Jujuy.

Lead Levels in Canadian Children: Do We Have to Review the Standard ?

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The trend in lead research is the documentation of biological effects at lower and lower levels of lead exposure with recurrent downward adjustments of 'safe' thresholds. Blood lead levels that were once considered safe, can adversely affect the neurodevelopment of children. A review of the Canadian literature was undertaken to examine reported information on lead exposure in Canadian children together with sources of exposure and outcomes. Chronic low levels of exposure were particularly sought. The results of the review showed that there has been limited surveillance of blood lead levels of Canadian children. Studies have been mainly carried out in high risk groups. Public health initiatives to remove environmental sources of lead have been very effective in minimizing childhood exposures to this toxic heavy metal, namely removing lead from gasoline. As harmful effects of lead may occur in children below the current regulatory standards the threat of potential sources, many of which may be unknown, remains. Further biomonitoring surveillance as a comprehensive lead survey in Canadian children is necessary to determine how many Canadian children may be affected by chronic low dose exposure to lead. Classification of lead exposure or its effects need to be a notifiable condition. Advocacy for legislation to limit the lead content of products to which children are exposed is needed. Education of parents and caregivers to identify the potential sources of chronic low dose exposure for children and their harmful effects is necessary. Regulatory standards need to be reassessed to better protect children.

Exposure to Phthalates in Male Newborn from Medical Treatments

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Although human exposure to plasticizers such as phthalates is generalized, some infants could be exposure at potentially toxic levels. The phthalates are sustancias with antiandrogen effect in animals of laboratory. The studies in humans are limited but the effects of phthalates have been observed that respon to this mechanism of action. We performed an observational study to assess in infants under invasive medical produres are more exposed to phthalates than the general population because of plazticizers used in medical devices. Urinary metabolites concentrations of the most commonly used phthalates, monomethyl phthalate (MMP), monobutyl phthalate (MBP), mono 2 etylhexyl phthalate(MEHP), monoethyl phthalate(MEP) y monooctyl phthalate(MOP) were measured in 30 newborns unser intensive therapy and 30 newborns from the normal maternity room.

Average urinary MEHP concentration was 46.82 micrograms/liter for newborns under intensive therapy and 5.19 micrograms/liter for children in maternity room ($p < 0.001$). MEHP is the primary metabolite of di-2(ethylhexyl)phthalate. Results from this exploratory study show higher exposure levels in the group of newborns under neonatal intensive therapy as compared to newborns in maternity room.

Child Risk Due to Carcinogens Exposure in a High Vehicular Movement Area

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Several research studies have been made over the past five years about the quality of life in an area in Vicente López, which stands out for being a commerce / urbanized area, with high vehicular movement (75,000 cars a day). The objective of this study was to analyze the risk factors on environmental pollution, that has a strong impact on the younger population. We measured the breathing fraction of a particulated material PM 10 and PM < 2,5 (to inhale); with a high volume sampling device with an scale impactator on ground level. The organic fraction was analyzed, prioritizing the HAP fractions (Soxhlet method; HPLC), and mutagenesis was evaluated with the Ames' Test. Because of the importance of benzene (Type II ARC carcinogen), an important role was given to it regarding the quality of the air. La results on the particulates materials were within the standards of international regulations (NAAQS): PM 10:150 ug/m³ y PM< 2,5: 65 um/m³. The risk of mutagenesis in the population is given by the small fraction of particulated material. The results obtained were three time higher than the ones from a reference area. Regarding the COVs, the xilene values (meta/para/orto: 5,2 mg/m³) were within the international standards, not being the same situation with benzene (Xmedia: 0,00478 mg/m³)

With the research studies that have been made so far, we can analyze the potential risk of the child population, given the carcinogen and mutagenic power that the pollutants found (MP, benzene, and HAP) have.

Organochlorine pesticides in human milk. experience in a perinatalogical hospital of autonomic city of Buenos Aires. Argentina. 2000-2004

Susana Der Parsehian

Hospital Materno Infantil R. SARDA

Aims: Maternal contamination by organochlorinated pesticides is a risk factor that influences the fetus and the newborn. Levels of organochlorinated pesticides residues in human milk is the purpose of this study.

Design: observational and descriptive study.

Population: two hundred and forty eighth mothers assisted at Ramón Sardá Maternity Hospital (Buenos Aires) not more than 20 days after birth.

Exclusion criteria were: HIV, and anticoagulation.

Predictive variables: maternal age, marital status, educational attainment, parity, alcohol, weight, height, gestational weight gain. Predictive variables (in human milk): dichlorodiphenyltrichloetane, endosulfan, mirex, dichlorodiphenyldichloroetane, hexachlorobenzene, oxi chlordane, cis-chlordane, beta hexachlorociclohexane, lindane, heptachloro epóxide.

Predicted outcomes: levels of organochlorinated pesticides in human milk will allow population as well as individual guidelines in order to diminish adverse perinatal outcomes.

Results: 91,5% (IC 95%- 87,4-94,4) of the 248 samples contained at least one kind of the organochlorine pesticides. The most frequent were p-p´DDE: 86,7% (IC 95 % 82-90))X: 8.98 ng/ml; hexachlorobenzene : 26,6% (IC 95% 21,5-32)X: 1.50 ng/ml; heptachlor epoxide: 25.4%(IC 95% 20-31)X: 1.27 ng/ml; beta hexachlorociclohexane: 23,0 % (IC 95% 18-28) X: 4.32ng/ml; and Chlordane : 15,7%(IC 95% 11,7-20,8)) Xo xiCLD: 1.49ng/ml.

Conclusion: In most of the samples of human milk (91.5%) studied it was found residues of organochlorine pesticides.

Healthy Environments with Clean Water for Healthy Children

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La presente comunicación surge del proyecto de investigación: “Promoción del hábitat con agua segura: prevención del hacre”. Constituye una investigación que por primera vez se realiza en Tucumán, con el objetivo de evaluar diversos efectos –neurotóxicos entre ellos – de arsénico (As) y fluor (F) en habitantes del Este tucumano -en especial sobre niños y adolescentes-, zona de contaminación de agua y suelo por estos metaloides. Investigación multidisciplinar, articula aportes conceptuales, instrumentales y humanos, de tres instituciones de la Universidad Nacional de Tucumán: Facultad de Bioquímica, Química y Farmacia, Facultad de Psicología y Facultad de Arquitectura y Urbanismo. El abordaje del objeto se realiza bajo metodología cuantitativa y cualitativa, sobre niveles biológicos, psicológicos, socioeconómicos, arquitectónicos y urbanísticos. Se presentan en esta ocasión algunas observaciones y evaluaciones realizadas en terreno. Se considera como especial relevancia de esta propuesta: la consideración de las múltiples variables intervinientes; la investigación de los efectos neurotóxicos de los citados metaloides; el carácter multidisciplinario de la misma; la acción intersectorial de diversas instituciones de salud, políticas, etc, de nivel nacional y provincial, vinculadas con la temática, que potencian la implementación del proyecto, al mismo tiempo que confieren la posibilidad de realizar transferencia de sus resultados a instancias políticas de gestión ambiental, con propósitos correctivos y de acción preventiva en especial en el campo de la salud.

Analysis of Phthalates in Pregnant Women and Children of the State of Mexico

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They have been removed compounds that it has been demonstrated have affectations to the health, therefore they have been introduced new forms of manufacture and new polymers, but is continued employing the added PVC of plasticants for many uses, one of these plasticants are the phthalates, that recently identified as possible endocrine disruptors, the use of these compounds go from pipeline to transport water, toys for children until equipment of medical use as bags to contain blood, equipment of dialysis etc.

Seeking the presence of dialquil phthalates as symptom of the exposition of the population has been analyzed the women and children urine. The analytical method personnel for this analysis were developed thinking about the infrastructure conditions that there is about Mexico, creating thus an economic methodology and easily reproducible in any laboratory that count on an equipment of chromatografy of gases coupled to mass spectrometry.

It was found the presence of the primary metabolites of these compounds, like mono etyl phthahate (MEP), mono etyl hexyl pthalate (MEHP), mono butyl phthalate (MBP), and mono octyl phthahate (MOP), in the urine of the analyzed women finding geometric mean of up to 57.3 mg/L in the case of the MOP until 6.3 mg/L in the case of the MEHP. This method was employment also to evaluate the exposition to phthalates for medical procedure and in a preliminary form we found that in the children urine exposed to therapy procedures, where are used medical PVC equipment, is found until the double of the concentration of phthalates that in not exposed children.

Blood Lead, Anemia, and Short Stature Are Independently Associated With Cognitive Performance in Mexican School Children

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Lead exposure and nutritional factors are both associated with cognitive performance. Lead toxicity and nutritional status are also associated with each other. We examined whether nutritional status variables account for part or all of the association between cognitive performance and lead exposure. First-grade children ($n = 724$) ages 6-8 y, attending Mexican public schools located in the vicinity of a metal foundry were asked to participate and 602 enrolled in the study. Blood lead, iron status, anemia, anthropometry, and cognitive function were assessed. Results from 7 standardized tests are presented here. The mean blood lead concentration was $11.5 \pm 6.1 \mu\text{g/dL}$ ($0.56 \pm 0.30 \mu\text{mol/L}$) and 50% of the children had concentrations $>10 \mu\text{g/dL}$ ($0.48 \mu\text{mol/L}$). The prevalence of mild anemia ($<124 \text{ g/L}$) was low (10%) and stunting ($<2 \text{ SD}$) was nonexistent (2.3%). In bivariate analyses, lead was negatively associated with 4 cognitive tests and was also inversely correlated with iron status, height-for-age Z scores, and head circumference. In multivariate models, the association between lead and cognitive performance was not strongly affected by nutritional variables, suggesting that the relation of lead to cognition is not explained by lead's relation to iron deficiency anemia or growth retardation. In multivariate models, hemoglobin concentration was also positively associated with Peabody Picture Vocabulary Test and Number Sequencing performance, whereas serum ferritin was negatively related to the Coding subscale of the Wechsler Intelligence Scales for Children-Revised Mexican Version (WISC-RM). Funded by the Spencer Foundation, Chicago, IL.

Concentrations of Total Mercury in Blood and Urinates and Fish Intake in Children, Pregnant Women and in Age Reproductive Residents of the Municipalities Bordering the Lake Chapala, Jalisco-Mexico

Mariana Irina González Fernández

As consequence of the present contamination in the Chapala lake, Jalisco Mexico (water, sediment and fish), it is sought to identify the concentrations of total Hg in the children, pregnant women and in reproductive age that they inhabit the border of the lake of you Chapala; through the exhibition biomarkers: it bleeds and urinates that they are exposed through the quantity, frequency, species, type and the habits of fish consumption.

Taking in consideration that some groups react from way peculiar to the exhibition to the mercury, in particular the fetus, the newly born ones and the minor, because the nervous system in development is very delicate, the necessity is deduced from to increase the investigation instances in Mexico in this item and to propitiate that the parents, the pregnant women and in reproductive age, have conscience of the possible damages that the consumed Hg causes through the diet. Therefore, this investigation seeks to generate possible hypothesis (cross sectional study) on the concentrations of Hg inside the organism soon after the fish consumption. Besides, observing the possible cases prevalence of the children's neurological damages, of the pregnant women and in reproductive age.

Detection of Contamination and Poisoning By Lead (Pb) in Infants of a Precarious District in Buenos Aires - Argentina

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Children from a precarious area located in 28th block of Villa 20, Buenos Aires City were studied. This land was filled up with garbage of unknown origin and classification, until the late 80's, when it was occupied by a car's cementery and at present by families. The fact that these lands could contain high level of contamination made us decide to carry out this study.

Objectives : Set blood lead levels (BLL) in the children population and investigate the association between clinical sings, laboratory results, and lead contamination or poisoning.

32 children from 9 month to 5 years old who live in 28th square were studied in October November 2004.

A Clinical protocol was designed for this population. Hematology parameters (Pinero Hospital) were made by automatic method , and BLL by Atomic Absorption Spectroscopy.

Results and conclusions : BLL < 7 ug/dl. : 68.9 % (20/29) ; BLL between 7 ug/dl. and 10 ug/dl : 17.9 % (5/29) ; BLL > 10 ug/dl. : 13.8 % (4/29); BLL Reference Value, less 10 ug/dl.

No Clinical differences were found between children with BLL > 10 ug/dl or less than 10 ug/dl. All children with BLL > 10 ug/dl. Have been dwelling for over a 24 month's period in this land. It would suggest that the source of contamination, should be attribute to the environment where they live. A ground study is suggested to have an environmental diagnosis of certainty.

Determination of Reference Values for Cholinesterase in Children in the Population around R. Gutiérrez Children's Hospital in the City of Buenos Aires

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Introduction: Plasmatic and erythrocyte cholinesterase are enzymes characterized by two main fluctuations, inter- and intra-individual, reflected in wide ranges of normality. This cause several difficulties regarding the interpretation of the results, if no basal levels have previously been recorded in the patient. Due to poor bibliographic resources and to the absence of information nationally, the objective was to establish reference values for plasmatic and erythrocyte cholinesterase in the populations that attends to Ricardo Gutiérrez Children's Hospital.

Materials and Methods: We selected 158 children and adolescents that concurred to the Hospital's Surgical Service for a programmed elective surgical treatment. Plasmatic cholinesterase was determined by the Knedel and Bottger Method, which uses Butyrylcholine as a substrate and Acetylcholinesterase was determined using a kinetic method, with Acetylcholine as a substrate (Ellman's Method), previously rinsed and lysis of red blood cells.

Results: For erythrocyte cholinesterase the mean value was 7823 UI/L of red blood cells, corresponding the 2.5 and the 97.5 percentiles to activities of 6056 and 10320 UI/L respectively. For the plasmatic cholinesterase the mean value was 11591 UI/L with activities of 7689 and 15056 UI/L corresponding to the 2.5 and 97.5 percentiles. No significance difference regarding sex and age were found.

Discussion: We consider it highly important to determine reference values for our population in order to understand correctly the levels of acetyl cholinesterase and cholinesterase in case of toxic or drug exposure that might affect the activity of these enzymes, or for the detection of non typical variants.

Pesticides Exposure among Students beside a Flower Plantation in Ecuador - Preliminary Results of the Health Effects

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A health survey was developed in a school allocated beside a flowerplantation which greenhouses are between 20 to 80 m. far from the classrooms of the school. Application of organophosphates and carbamates pesticides is frequent (1-3 times a week). A statistical representative sample of the students (140 students) was studied. A questionnaire asking for exposure to pesticide and health effects was applied. A clinical and neurological examination was performed to each student. Erythrocyte Acetyl Cholinesterase test was done with the EQM Research equipment (Ellman modified method). WHO Neurobehavioral Core Test Battery abbreviated was used to study neurobehavioral disorders : Santa Ana dexterity test, Benton Visual Retention, Digit Span, Pursuit Aiming, Trails A and B. Peripheral sensitivity was measured with Vibraton II.

Preliminary results show moderate exposure of the students, in particular those who are seated in the classroom close to the plantation. Health effects as the presence of headache, nauseas, , vertigo, sickness, cough, abdominal pain, were frequently mentioned. AChE results lower than the reference values accepted and low performance in some tests were found. Confounders as use of pesticides at home, alcohol consumption and neurological diseases were considered. The study of presence of pesticides in soil and dust and the analysis of metabolites of pesticides in urine are in process. Preliminary results initially confirm exposure of the students and health effects showed by similar studies. Preventive measures and stronger controls are need to avoid this problems in the students.

DNA Damage in Children Exposed to DDT in a Malarious Area of Chiapas, Mexico

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DDT [1,1,1-trichloro-2,2-bis(p-chlorophenyl)ethane] was widely used in Mexico for the malaria control program. Therefore, in this study, the potential DNA damage associated with exposure to DDT and DDE of 30 children living in DDT sprayed areas of Chiapas, México was assessed using Cometa Assay. The results were compared with 30 controls of comparable age and sex, who were living in areas less exposed to DDT. Samples of whole blood were obtained to measure DDT, DDE and to carry out the Comet Assay. The children living in DDT sprayed areas had significant greater means of DDT and DDE than controls, obtaining 15.9 ± 8.2 and 58.24 ± 29.2 $\mu\text{g/L}$ respectively, whereas controls had 1.9 ± 3.6 and 9.2 ± 5.7 $\mu\text{g/L}$, respectively. There was also statistically significant differences in comet tail's mean length between the two groups examined (mean 26.83 ± 6.05 versus 17.13 ± 3.69 μm , $p < 0.001$) and tail moment (mean 7.13 ± 2.9 versus 1.21 ± 2.19 , $p < 0.001$). Regression analysis showed a positive association between blood levels of DDT, DDE and DNA damage, measured as comet tail length (DDT $r^2 = 0.54$ and DDE $r^2 = 0.64$, $p < 0.001$) and tail moment (DDT $r^2 = 0.51$ and DDE $r^2 = 0.56$, $p < 0.001$). The findings of the present study suggest that exposure to DDT and metabolites in DDT sprayed communities can cause DNA damage.

Clinical Evaluation and Genotoxicity Biomarkers in a Children and Adult Population Exposed to Many Pesticides

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We have studied the infantile exhibition to pesticides according to the processes that were made in the family and the surroundings, near the community of Bella Union, Uruguay. The objective is to know the prevalence diseases and genotoxic alteration of the population that lives and works around fruit and vegetables crops, and sugar cane, or rice crops. A group of 60 people (20 children) were recluted, being 275 persons the whole population.

An environmental clinical history was made, along with cholinesterase, chromosome aberration's test, Cometa Assay, and percentage of apoptotic cells. 50% of the people that we studied live less than 250 meters from the crops, and the use of the pesticides is every tree days in average. The most common pesticides used are: Carbofuran, 2-4D, Glyphosate, Chlorpyrifos, Cypermethrina, Endosulfan. The prevalence of respiratory diseases was of 15 % in adults and 63% in children, of skin diseases 14.5% in adults and 37% in children. 40% of the women have reproductive pathological antecedents. The DNA damage index (Cometa Assay) in men was 1.80, in women 2.20 and in children 2.44; the percentage of apoptotic cells was 0.30 in men, 0.26 in women and 0.42 in children; the chromosomic aberration rate was 4.44 in men, 5.54 in women and 5.67 in children. The results show that in children there is a very important prevalence of respiratory and skin diseases. They also show a tendency to DNA damage in children and women, which implies the existence of greater vulnerability in children. New studies are required in order to be able to value the meaning of these results.

Neurotoxic Effects from Chronic Exposure to Pesticides in Children

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Neurotoxic effects of the chronic exposition to insecticides in children. Various works exist that have shown the vulnerability of the nervous system before diverse types of insecticides. But these works, in their great majority, have analyzed the effect of the sharp exposition to these toxic in the places of work. Nevertheless, with these agricultural workers we find their families. They accompanies them in this to emigrate from one to another plantation. And, in these family contexts, a large quantity of childlike population exists that, despite that many times they are not exposed to large quantities of toxics in a sharp way, they are exposed to small but repeated expositions.

The INQA group, decided to investigate the effects neurotoxics of the chronic exposition to insecticides in the childlike population. The purpose is to detect subtle changes in the nervous system, that not be controlled and reverted on time, can culminate in damages more severe and irreversible.

The present work presents the collection of the results obtained in the area. These results although even are tentative they are promising. The fact that they begin to be observed since early age and that the first one in being affected is the peripheral nervous system, give us hopes. It is possible that with an early detection and intervention in the healthy environment, with the purpose of stopping and to revert the damages produced by these toxic, we can avoid greater problems; if the exposition continues the central nervous system and upper functions can be damaged, as well as the memory.

DNA Damage Associated with Urinary Arsenic Content in a Child Population Exposed to Arsenic through Drinking Water

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Arsenic is an environmental pollutant widely distributed in the world. In Argentina about three million of inhabitants are exposed to its deleterious effect by drinking water with high levels of this metalloid.

In this work the correlation between the exposure to inorganic arsenic and the level of DNA damage in blood cells was assessed. Urine and blood samples were taken from a population of Santiago del Estero province and urinary total arsenic (Asu) content (as a recent exposure biomarker) and single cell gel electrophoresis (Comet assay) were performed. Children represented the 44% of the sampled population (n=64) and 57% of them had Asu levels between 41.78 and 3918.10 $\mu\text{gAs/g creatinine}$ (reference value: less than 40 $\mu\text{gAs/g creatinine}$). Comet assay showed that children with high level of Asu presented a high percentage of DNA damage (32.79 ± 1.92) compared with those with Asu below the reference value (9.76 ± 4.66).

Despite the small number of samples analyzed in this preliminary study, there is a clear tendency of correlation between total arsenic content in urine and DNA damage. The data obtained showed that the children population exposed to high levels of arsenic, represent a group of risk for developing pathologies related with this toxic.

La Plata's Air Pollution: Risk Factors and Respiratory Pathologies in Children

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The objective of this project consists in establishing the associations between environmental factors and respiratory pathologies with an obstruction component in children. Particularly the epidemiologic survey that we applied, stands out (1,200, over ISAAC basis) for the study of environmental conditions and public health, for the measurement of respiratory capacity in the children that took part in this study, and the determination of volatiles organic compounds (COVs) in the intra-wall or the extra-wall air, on the basis of a previous chemical, mutagenic and citotoxic characterization, of the environmental air in the area (L. Massolo's doctorate thesis, 2004)

This project counted with the participation of several professionals from Hospital de Niños de La Plata (F. Winchmann), from Trabajo Social – Social Work (A. Carballeda, F. Barberena, V. Chiapperiniy M. Martín) and from the Centro de Investigación de Medio Ambiente – CIMA (Environmental Investigations Centre) (A. Porta, N. Cianni, L. Massolo), the last ones from Universidad Nacional de La Plata. (UNLP)

The research project takes place in neighbors areas, with known sources of COVs (Petrochemical Pole – PP – and Urban Helmet – UH – with high vehicles circulation), and in areas with low Extra-wall – outdoor levels of COVs (residential – R – and semi rural – SR –) At the moment, all of the surveys provided for PP and SR, have been completed; the 50% of UH, meanwhile in R it was completed, with school intervention. In Epi – Info about 750 surveys were loaded (65%) The preliminary statistical analysis shows statistical correlation between the respiratory disease and the nearness to PP. The PP and SR spirometries were completed. All of the COVs monitors were placed in August (30 days before exposure)

Organochlorine Pesticides Residues in Infant Milks and Their Risk Evaluation

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Dates about intake of pesticide and the risk evaluation for children do not exist in Argentina, neither exist information about general food with pesticides in baby foods, and how much contribute to the ADI.

It was investigated residues of organochlorine pesticides in 50 milk and 51 milk products samples, specially manufactured and recommended for neonates and babies, it was calculated the Estimate Daily Intake (EDI) on the basis of these foods consume and body weigh and it was compared these results with the ADI (FAO). The samples were collected at local markets in the Buenos Aires, during the period of February 2001 to December 2003.

Investigation was made by gas chromatography with electron capture detectors and automatic injector.

The results were expressed in ug/ml and it was considered the next groups: Aldrins; Chlordane; DDT; Endosulfan; HCH; Heptachlor; Endrin; HCB and Lindane. Of 101 analyzed samples, 10% did not contain pesticides residues, 24.8% contained at least one pesticide, 19.7% contained two and 2% showed evidence of seven and eight organochlorine pesticides. Within all pesticides groups investigated Aldrins and DDT had representative percentages (32%), and Heptachlor (57%) and HCH (53%) the more elevated frequency. In milk samples the contribution to the ADIs when it was considered neonates were: Heptachlor ranged from 11100% to 1306% and Aldrins from 3000% to 285% at maximal and mean levels. In milk products Heptachlor overcome the ADI 6.38 times when it is taking account neonates and maximal concentration and for mean and median concentration the contribution to the ADI were 81% and 60% respective.

Biomarkers for Monitoring Intrauterine Organophosphate Pesticide Exposure in Rural Communities

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Improvement of children's health requires preventing environmental exposures and identifying predictive biomarkers that represent the toxicological process before irreversible injury appears. Considering the high vulnerability of the intrauterine development, this study was designed to investigate the impact of in utero exposure to organophosphate pesticides and biomarkers of early effects in easily accessible tissues. A cohort of 342 women living in the agricultural area of High Valley of Río Negro and Neuquén, where 6 month spraying and non spraying periods are alternated, were interviewed in order to characterize their demographic characteristics and lifestyle habits. Morphometric information about the offspring and placentas were recorded. The analytical studies included pregnant women hemogram, blood cholinesterases as well as placental enzymes activities. Data were analyzed by MANOVA, multiple regression and correlation. During spraying season plasma cholinesterase diminished significantly (18%) and was associated to exposure length. In this period, placental acetylcholinesterase (AChE) and catalase (CAT) increased in a similar extent (40%) and gestational age diminished in two weeks. An increase in cephalic circumference was observed in newborns from women residents in rural areas and also in ones having indoors fumigation habits. This parameter was associated to CAT activity. These results indicate that the combined use of the placental AChE and CAT, enzymes involved in adaptative events, seems to be a useful tool in environmental monitoring programmes. Also, they corroborate that this tissue, the most accessible and available component of the triad mother-infant-placenta shows cumulative effects that reflect the intrauterine environment in which the newborn was developed.

Living near Mining Waste is Associated with Higher Blood Lead Concentrations in Children

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Objective: Our aim was to identify the association between proximity of residence to mining site waste (tailings) and blood lead concentration (PbB) in children.

Materials and Methods: We conducted a cross-sectional study in May 2000 in four socioeconomically similar towns in the State of Guerrero, Mexico. The study population comprised 156 children ≤12 years of age grouped into three communities (A-C) near mining waste site (n = 115) and one additional community (D) located >25 km from the mining waste site (n = 41). PbB was measured by anodic voltammeter and exposure factors (demographic and environmental) were collected by questionnaire.

Results: Geometric mean PbB was 8.2 g/dl (95% confidence interval [CI] 5.2, 11.1 g/dl), 8.1 g/dl (95% CI 5.5, 10.6 g/dl), and -0.3 g/dl (95% CI -2.9, 2.4 g/dl) for the three proximal communities and -2.9, 2.4 g/dl (95% CI -2.6, 2.2 g/dl) for the distant control; differences between proximal and distant groups were statistically significant (p <0.001). Multivariate regression models were used to estimate adjusted mean differences, explaining 41% of blood lead variability with the following variables: cooking in lead-glazed ceramicware, β = 0.54, p <0.05; sex β = 0.79, p = 0.6; age β = 0.081, p <0.001; community A, β = 1.07, p <0.001; community B, β = 0.96, p <0.001, and community C, β = -0.07, p >0.05, the three communities referenced against the distant community (D). To assess the impact of the different variables regarding risk of having high blood lead levels, we categorized the dependent variable PbB with cut-off points ≤10 g/dl and >10 g/dl and conducted the analysis with logistic regression. Children living <5 km from mining waste sites had increased odds of PbB of >10.0 g/dl (community A: odds ratio [OR] =7.3, 95% CI: 2.1-25.1; community B: OR = 80.5, 95% CI, 9.7-665.9, and community C: OR = 0.7, 95% CI, 0.2-2.1) compared with the control-group community.

Conclusions: Children living near mining waste had higher PbB than children residing in comparable communities distant from mining waste sites and this increased the odds of having PbB >10 g/dl. Our results are comparable to similar studies in other countries.

Asthma in Under-Privileged Populations is Mainly Non-Atopic. Impact on Current Management Strategies like IMCI From PAHO/WHO

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Data from recent ISAAC studies in Latin American countries show high asthma prevalence in children. Asthma is associated with atopy in populations from developed countries. One possible explanation is that early life infections, like parasitosis, in more “hostile” environments may be protective. Mechanisms associated with asthma and its relation with their environments in children of under-privileged populations may thus be unique. **Methods** A total of 1982 children aged 9-13 years were randomly selected among students from public schools of a poor Southern Brazilian town. Parents answered a complete ISAAC-standard questionnaire on asthma, and known environmental risk factors. 1135 children had skin-prick tests for common aeroallergens. A subgroup of 643 children had parasitological stool exams. **Results** Children had mean age of 10.2 years and 6.2% had a previous history of “bronchiolitis” at age 2 years. Wheezing in the previous 12 months was positive for 26.4% and current asthma prevalence was 9.4%. Of all children tested 13.7% had at least one positive skin test. 29% of current asthmatics had at least one positive skin test and this rate was 21.3% among current wheezers. There was a significant inverse association between parasitosis and atopy, especially for helminthic infections (OR, 95% CI: 0.5, 0.2-0.9). Instead, Giardia was positively associated with non-atopic wheezing (OR, 95% CI: 2.0, 1.1-3.5). Most significant risk factor for atopic wheezing was maternal history of asthma. Most significant risk factor among non-atopic wheezing is a positive history for an event of bronchiolitis early in life (OR, 95% CI: 16.7, 9.3-29.9). **Conclusions** Non-atopic wheeze is most prevalent clinical phenotype. Helminthic infections are protective for atopy while Giardia is associated with non-atopic wheeze. These results suggest that strategies aimed at treating asthma may have to be tailored for these different phenotypes.

A Proposal to Establish a New Screening Method to Detect Potential High Risk Group in the Next Generation

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We have reported that human fetuses are contaminated by many persistent and non-persistent chemicals through the research using umbilical cord (Todaka and Mori, *Congenital Anomalies*, 2002; Fukata et al., *Environmental Health Perspectives*, 2005; Omori-Inoue et al., *ISPAC*, 2005; Todaka et al., *Environmental Research*, 2005). Several studies suggest that fetal exposure to organochlorine pollutants might cause adverse effects on human development. Therefore, it is necessary to find potential high risk group to prevent those adverse effects. We suggest using the data of the concentration level of total PCBs in maternal serum to predict the contamination level of the sum of organochlorine chemicals in fetuses since we found the correlation between them. It is recommended to use the conventional method of measuring serum PCB level, packed column gas chromatograph - electron capture detector (packed column GC-ECD), which has been the official method to measure the total PCBs in Japan, because the method is simpler and less expensive than high-resolution gas chromatography - high-resolution mass spectrometry (HRGC-HRMS)(Todaka et al., *ISPAC*, 2005). If a screening is conducted in a group of women at reproductive age, potential high-risk group who accumulate organochlorines at higher level can be detected. Furthermore, if proper treatment is performed to them, then it may be able to prevent adverse health effect on the future generations. In our presentation, we will summarize our published and unpublished data and suggest a new method of assessment of potential high risk group and also suggest establishing a preventive medicine for future generations.

Effects of Prenatal P,P'-DDE Exposure and Breastfeeding on Infant Neurodevelopment .

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DDT was extensively used in Mexico, evidence about the effect of prenatal P,P'-DDE (DDT'S main metabolite) exposure on early human neurodevelopment is scarce and contradictory.

To evaluate the impact of prenatal p,p'-DDE exposure on psychomotor (PD) and mental development (MD) of infants, 214 children were identified (single pregnancies, without complications during labour) from an ongoing perinatal cohort study in Morelos, Mexico. Serum p,p'-DDE levels during pregnancy were measured by gas-liquid chromatography. PD and MD at one, three, six and twelve months of age were assessed through the Bayley Test (BSID-II). A multivariate analysis with mixed effect models was performed to estimate the impact of prenatal p,p'-DDE exposure and lactation on neurodevelopment.

The geometric means of p,p'-DDE at each trimester of pregnancy were 6.32 , 6.7 and 7.8 ng/ml respectively with a total range of 0.42 - 115.7. In the PD area, the averages of the BSID-II were similar in each child evaluation, with a global mean of 92.8 SD 8.5; likewise, the observed value for MD area was of 96.2 SD 5.5. As expected, only the levels of p,p'-DDE during the first trimester of pregnancy were negatively associated to MD (significant reduction of 0.15 points, for an increase of almost 3 ng/ml of p,p'-DDE) and PD (0.89 points) where never breastfed children had higher reduction (1.62 points) than those who were lactated (0.65 points) (p for interaction <0.001).

The reversibility of breastfeeding protection on PD impairment due to in utero P,P'-DDE exposure needs to be evaluated in further longitudinal studies.

Biomarkers of Environmental Tobacco Smoke Exposure in Argentina

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Developing appropriate measurement methods for environmental tobacco smoke exposure (ETS) has attracted increasing interest as a result of the accumulating evidence of the ill effects of ETS on human health. Questionnaires have been the usual method used to assess exposure of ETS and its association to illness. However, questionnaires have drawbacks such as recall bias and low sensitivity, which may lead to inaccuracy in the interpretation of associations between ETS and illness.

We are to measure the prevalence of second hand smoking in groups of children at risk in Mar del Plata city through biomarkers of exposure to environmental tobacco smoke as urine cotinine and hair nicotine by gas chromatography and high performance liquid chromatography (HPLC) respectively and study its correlation with questionnaire assessment of exposure to ETS. On the other hand we are to surveillance nicotine in commercial cigarettes in Argentina and developed new method of detection by capillary electrophoresis.

Our results will contribute to development and implement protective measure by environment and people and to reinforce epidemiological surveillance of related diseases.

Lead Blood Levels and Neuro-Behavioral Effects in Children Ages Three to Eight

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The objective of this work was to identify the neuro-conductual disorders of a group of children between 3 and 8 years old, with lead blood levels equal or above 10 ug/dl. This cross-work study was held between April and December 2002, 125 children, both male and female, from a section of Havana, the Consejo Popular "Los Sitios," in the City of Havana were selected because they were aged 3 to 8, were exposed to several environmental risks factors (living in old and deteriorated houses, built before 1928, similar collapsed houses nearby, in which terrain children played, construction ceters) as wells as personal risks factors (playing with lead toys, chewing color pencils, etc.) All children were screened for lead levels in cappilar blood. Of all the children studied 55 were sent for a toxicology consult, for neurobehavioral study, but only 52 of them were able to complete the studies. The neurobehavioral changes that were identified were: aggression, irritability, lack of concentration, IQ, attention deficit, and bradipsychia. We found out that 42% of the children between 3 and 8 years old with lead blood levels of 10 ug/dl or more presented with neuro-conductual problems.

The Otoacoustic Emissions, a Biomarker of Ototoxic Effect, Proved Association between Environmental Exposure to PCBs and Hearing Impairment in 8-9 Year-Old Children

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In Slovakia a chemical plant produced PCBs between 1959 and 1984. Disposal of effluent into a river resulted in contamination of environment, recognized as one of the areas all over the world most heavily polluted with PCBs. The data for sum of PCB serum concentration (ng/g serum lipids) for 433 8-9 years old children are: mean 528.2, median 321 and limits of the quartiles-18, 175, 321, 618, 6477. Hearing examination involving pure tone audiometry, transient evoked otoacoustic emissions, auditory brainstem response and tympanometry, was added to the schedule as auditory thresholds for 1-kHz tones were reported to be elevated by approximately 25 dB in PCB exposed animals (Goldey 1995) and were linked to a loss of outer hair cells (Crofton et al. 2000). The main findings were: An association between negative middle ear pressure and PCB serum concentrations and increases of the hearing thresholds at low frequencies, no associations between the serum PCB and any of the auditory brainstem response parameters and increasing serum PCB associated to decreasing emission level of the transient evoked otoacoustic emissions.

The sound pressure level of otoacoustic emissions was associated with results of several neurobehavioral tests applied in the same cohort and proportion of permanent teeth with demarcated, diffuse opacities or hypoplasia. Obtained data confirm EC document (COM (2001) 593 final) stating that new epidemiological, toxicological and mechanistic data have emerged which indicate that dioxins and some PCBs have a broader impact on health than previously assumed.

This work has been completed within the project PCBRIK supported by the European Community under the contract No. QLK-CT-2000-00488.

An Indicator Model For Children's Environmental Health in Argentina

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The Canadian Institute of Child Health (CICH) and the Asociación Argentina de Médicos por el Medio Ambiente(AAMMA), in cooperation with a number of Canadian and Argentine partners, is working together in a multi-disciplinary process involving the public and non-governmental sectors, to complete a Profile that collects and compiles information on the state of Children's Environmental Health in Argentina. This initiative is funded by the Canadian International Development Agency (CIDA).

The project has chosen an ecological model on which to build its indicator framework. This is based on the Multiple Exposure-Multiple Effect (MEME) model. The project's unique approach identifies context indicators, health and well-being indicators and exposure indicators. This framework recognizes that the context within which children learn and grow influences their health and development. This contextual domain can be thought of as the "inputs" - or the circumstances within which children live that influence their health, well-being and developmental outcomes. These are things like their socio-economic status, access to food and nutrition, etc. The framework goes on to identify both health and well-being or "outcome" indicators and environmental exposures. This recognizes that determinants and exposures do not act in isolation - but interact in complex ways.

Effects of Arsenic and Fluoride on Central Nervous System

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Millions of people around the world are exposed to arsenic (As) and/or fluoride (F) through drinking water (DW). In Mexico, approximately 6 million of people are exposed to both pollutants; from these 35% are children. Experimental and epidemiological studies support the evidence that both pollutants are neuro-toxic. They have the ability to cross the blood brain barrier and to accumulate in the brain. Nevertheless, one of the worrisome effects is the reduction of the intelligence quotient (IQ) (Li X.L, 1995; Zhao L.B, 1996, Lu Y; 2000, Calderón, 2001, Wasserman, 2004). In the center-north of Mexico the As and F levels in DW are superior to the established values in the *Norma Oficial Mexicana* (NOM SSA1-027). We designed a cross-sectional study in children, to evaluate the effect of the exposure to As and the F on the IQ and the neurological functions in children. One-hundred thirty two children from 6 to 10 years were included in the study from four communities with different As and F concentrations in DW: 1) Soledad de Graciano Sánchez, San Luis Potosí, (SLP) (As 6.7 ± 1.2 mg/L; F 0.7 ± 0.3 mg/L); 2) Moctezuma, SLP (As 4.5 ± 1.5 mg/L; F 1.1 ± 0.01 mg/L); 3) Salitral de Carrera, Villa de Ramos, SLP (As 169.5 ± 16 mg/L; F 5.3 ± 0.18 mg/L and 4) 5 de Febrero, Durango (Dgo) (As 200 ± 84 mg/L; F 9.4 ± 1.1 mg/L). Two neuropsychological tests were applied; 1) The Weschler Intelligence Scale revised version for Mexican children (WISC-RM) to evaluate, the IQ (verbal, performance and full), as well as cognitive functions (like attention, memory, visuospatial organization and language), and 2) The Rey-Osterrieth Complex Figure Test (ROCF), to evaluate visuo-spatial organization and short term memory. As exposure biomarkers As and F in urine were analyzed by atomic absorption spectrophotometry. As confounding factors lead in blood (PbS), socioeconomic status (SES) and nutritional evaluation (anthropometric measurements and iron deficiency) were evaluated. After adjusting by confounding factors, inverse associations between As and the F in urine and the scores of Full IQ, verbal IQ, performance IQ and the ROCF were obtained. These results suggest that the chronic exposure to both pollutants affects the higher brain functions in these children.

Genotoxicity in Blood Cells from Children Living in a Mining Area

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In México there are many areas with high arsenic and lead concentrations in soil, associated with the mining. The Villa de la Paz-Matehuala site shows a heavily polluted area directly related to the mining activities developed during the last 200 years, five tailing impoundments have been installed around the town and this deposits contain complex mixtures of metals; the most important are arsenic and lead. Arsenic is a well documented to increase the risk of humans carcinogen and the lead is know neurotoxin in children. The objective of this study was to assess the concentration of urine arsenic and blood lead in children living in the zone Villa de la Paz-Matehuala, also was evaluate the DNA damage in blood cells used the comet assay. The study was conduced among 55 children ages 4-11. We used first-void urine samples and venous blood. The arsenic and lead analyses were carried out with atomic absorption spectrophotometric. Comet assay was performed putting a fresh blood sample in a layer of agarose, after the cells were lysed and electrophoresis was performed. After the electrophoresis, the slides were stained and DNA damage was analysed using epifluorescent microscope. The children living in Villa de la Paz-Matehuala had urinary arsenic and blood lead levels higher. The half samples had arsenic levels higher than 50 Ug/g creatinine and lead above 10 ug/dL (CDCs action levels). The results of the comet assay showed that the tail moment in children living in this area were higher than other children.

Environmental Smoke and Child Health

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Children affected by parental smoking are exposed to many health problems. The impact is serious and it begins before birth.

Objectives: 1) To determine the incidence of children exposed to parental smoking at home among our patients. To investigate not only respiratory problems among their mothers and the aggravation during pregnancy, delivery and puerperal time, but also the incidence of sudden death.
2) To promote a home free from smoke for our patients

Material and Methods: A semi-structured questionnaire for 100 mothers of patients who consulted at the Zubizarreta Hospital and the CAPS Andes Army between March and June, 2005.

Results: There were only 28 families without smokers, 30 smoking mothers and 42 families with smoking fathers or relative at home. Smoking mothers had a higher incidence of spontaneous abortions, preterm births, low weight newborns and perinatal complications, and also more cases of sudden death in children.

Their children had a higher incidence of otitis media, frequent coughs, bronchiolitis, obstructive bronchitis, pneumonia and hospitalization by respiratory cause, similar to the group with other smokers. The difference was statistically significant comparing them with homes without smoking. Among these there was 42% children who had not any of these diseases, compared with 6.6% in families with smoking mothers and 14% at homes with other smokers, and this also represents a significant statistical difference.

Conclusions: Most of our patients are exposed to smoking considering the numerous problems that this causes, without forgetting the enormous additional costs to the sanitary system. We should insist in our character of health workers on the importance of achieving a free smoke home for all children.

Apoptosis and Oxidative Damage to DNA in White Blood Cells in Children Exposed to DDT and its Metabolites

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In previous studies, we showed that DDT and its metabolites are able to induce apoptosis of peripheral blood mononuclear cells (PBMC) in vitro. Moreover, we have demostred that the oxidative stress is the mechanism for which DDT and its metabolites induce apoptosis in vitro. For this reason, we performed a study in children exposed to this insecticide to evaluate the property to induce apoptosis in vivo (as a biomarker for exposure to DDT and its metabolites). A significant association between DDE, and Total DDT blood levels and apoptosis percentage was found in children with different levels of exposure. However, the mechanism for which DDT generates apoptosis in vivo has not been elucidated. In a posterior study we used a modification of the comet assay to evaluate of oxidative damage to DNA in children exposed to DDT and its metabolites. We detected DDE (3.81-174.52 µg/L) in all children monitored, while for DDT and DDD levels ranged from no detectable (nd) to 37.68 and 9.71 µg/L respectively, while for the evaluation of DNA damage using the comet assay, we observed damage to DNA in children exposed to DDT and its metabolites (tail moment between 4.13 to 16.90). Moreover when the cells of children exposed were treated with the formanidopyrimidine-DNA glycosylase enzyme (FPG), an enzyme detecting oxidized purines in DNA, gave rise to a significant increase in the extent of DNA damage. Our data indicate that children exposed to DDT and its metabolites present apoptosis and oxidative damage to DNA in immune cells. Those effects can use as biomarkers for exposure to DDT and its metabolites.

Can Behavioural Change Reduce Indoor Air Pollution Exposure and Improve Child Respiratory Health amongst Children Less Than Five in Developing Countries?

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Indoor air pollution (IAP) is causally associated with child ALRI and is the fourth largest killer of young children in developing countries. The sustainability of expensive technological interventions (such as cleaner fuels and stoves) has been questioned in poor rural areas. Behavioural change may offer a cheaper alternative but has yet to be scientifically evaluated. The aim of this study was to determine the impact of a behavioural intervention on a) child exposure to IAP and b) child respiratory health in a poor rural village in South Africa. A cohort of children <4 years old (N=502) were recruited and allocated to either an intervention (n=244) or control group (n=258). Results showed that the two groups were well balanced at baseline in terms of socio-economic status, exposure indicators (PM10 [kitchen], CO [kitchen] and CO [child]) and child respiratory health. The intervention (which promoted three simple behaviours) was implemented amongst primary caregivers in the intervention group after the baseline assessment. Follow-up visits (12 months later) showed significant reductions (in the order of 50%) in adjusted child indoor air pollution exposure indicators amongst the intervention group but limited reductions amongst the control group. Results showed no protective effect on respiratory health related morbidity (OR=1.79) or mortality (OR=1.23) possibly due to the limited power of this study. However, a published exposure-response curve suggests that reductions described in this study should result in respiratory health benefits. This is the first study worldwide to highlight the IAP reducing potential of behavioural change in developing countries - the implications of which will be discussed in the presentation.